

CLAIMS

1. A polypeptide, which polypeptide:

(i) comprises or consists of the amino acid sequence as recited in SEQ ID NO: 10, SEQ ID NO: 14, SEQ ID NO:16, SEQ ID NO: 18, SEQ ID NO: 20 and/or SEQ ID NO: 22;

5 (ii) is a fragment thereof which functions as a biologically active polypeptide and/or has an antigenic determinant in common with the polypeptides of (i); or

(iii) is a functional equivalent of (i) or (ii).

2. A polypeptide which is a functional equivalent according to part (iii) of claim 1, characterised in that it is homologous to the amino acid sequence as recited SEQ ID 10 NO: 10, SEQ ID NO: 14, SEQ ID NO:16, SEQ ID NO: 18, SEQ ID NO: 20 and/or SEQ ID NO: 22, and is a leucine rich repeat containing polypeptide.

15 3. A fragment or functional equivalent according to any one of the preceding claims, which has greater than 50% sequence identity with the amino acid sequence recited in SEQ ID NO: 10, SEQ ID NO: 14, SEQ ID NO:16, SEQ ID NO: 18, SEQ ID NO: 20 and/or SEQ ID NO: 22 or with active fragments thereof, preferably greater than 60%,70%, 80%, 90%, 95%, 98% or 99% sequence identity.

20 4. A functional equivalent according to any one of the preceding claims, which exhibits significant structural homology with a polypeptide having the amino acid sequence given in SEQ ID NO: 10, SEQ ID NO: 14, SEQ ID NO:16, SEQ ID NO: 18, SEQ ID NO: 20 and/or SEQ ID NO: 22.

25 5. A fragment as recited in any one of the preceding claims, having an antigenic determinant in common with the polypeptide of part (i) of claim 1 which consists of 7 or more (for example, 8, 10, 12, 14, 16, 18, 20 or more) amino acid residues from the sequence of SEQ ID NO: 10, SEQ ID NO: 14, SEQ ID NO:16, SEQ ID NO: 18, SEQ ID NO: 20 and/or SEQ ID NO: 22.

6. A fusion protein comprising the polypeptide according to any one of the preceding claims.

7. The polypeptide of claim 6, wherein said polypeptide comprises a histidine tag.

30 8. The polypeptide of claim 7, whose sequence is recited in SEQ ID NO: 24, SEQ ID NO: 26, SEQ ID NO: 28, SEQ ID NO: 30, SEQ ID NO: 32, and/or SEQ ID NO 34.

9. A polypeptide according to any previous claim which is glycosylated.
10. A polypeptide according to claim 9 which has the sequence referred to in SEQ ID NO: 10 and is glycosylated at one or more sites selected from amino acid 45, 115, 454, 746 and 756.
- 5 11. A purified nucleic acid molecule which encodes a polypeptide according to any one of the preceding claims.
12. A purified nucleic acid molecule according to claim 11, which comprises the nucleic acid sequence as recited in SEQ ID NO: 9, SEQ ID NO: 13, SEQ ID NO:15, SEQ ID NO: 17, SEQ ID NO: 19 and/or SEQ ID NO:21, or is a redundant equivalent or fragment thereof.
- 10 13. A purified nucleic acid molecule according to claim 11 or claim 12 which consists of the nucleic acid sequence as recited in SEQ ID NO: 9, SEQ ID NO: 13, SEQ ID NO:15, SEQ ID NO: 17, SEQ ID NO: 19 and/or SEQ ID NO:21, or is a redundant equivalent or fragment thereof.
- 15 14. A purified nucleic acid molecule which hybridizes under high stringency conditions with a nucleic acid molecule according to any one of claims 11 to 13.
15. A vector comprising a nucleic acid molecule as recited in any one of claims 11 to 14.
16. A host cell transformed with a vector according to claim 15.
17. A ligand which binds specifically to a member of the leucine rich repeat containing 20 family of proteins according to any one of claims 1 to 10.
18. A ligand according to claim 17, which is an antibody.
19. A compound that either increases or decreases the level of expression or activity of a polypeptide according to any one of claims 1 to 10.
20. A compound according to claim 19 that binds to a polypeptide according to any one of 25 claims 1 to 10 without inducing any of the biological effects of the polypeptide.
21. A compound according to claim 20, which is a natural or modified substrate, ligand, enzyme, receptor or structural or functional mimetic.
22. A polypeptide according to any one of claims 1 to 10, a nucleic acid molecule according to any one of claims 11 to 14, a vector according to claim 15, a host cell

according to claim 16, a ligand according to claim 17 or claim 18, or a compound according to any one of claims 19 to 21, for use in therapy or diagnosis of disease.

23. A method of diagnosing a disease in a patient, comprising assessing the level of expression of a natural gene encoding a polypeptide according to any one of claims 1 to 10, or assessing the activity of a polypeptide according to any one of claims 1 to 10, in tissue from said patient and comparing said level of expression or activity to a control level, wherein a level that is different to said control level is indicative of disease.
24. A method according to claim 23 that is carried out *in vitro*.
- 10 25. A method according to claim 23 or claim 24, which comprises the steps of: (a) contacting a ligand according to claim 17 or claim 18 with a biological sample under conditions suitable for the formation of a ligand-polypeptide complex; and (b) detecting said complex.
26. A method according to claim 23 or claim 24, comprising the steps of:
 - 15 a) contacting a sample of tissue from the patient with a nucleic acid probe under stringent conditions that allow the formation of a hybrid complex between a nucleic acid molecule according to any one of claims 11 to 14 and the probe;
 - b) contacting a control sample with said probe under the same conditions used in step a); and
 - 20 c) detecting the presence of hybrid complexes in said samples; wherein detection of levels of the hybrid complex in the patient sample that differ from levels of the hybrid complex in the control sample is indicative of disease.
27. A method according to claim 23 or claim 24, comprising:
 - a) contacting a sample of nucleic acid from tissue of the patient with a nucleic acid primer under stringent conditions that allow the formation of a hybrid complex between a nucleic acid molecule according to any one of claims 11 to 14 and the primer;
 - b) contacting a control sample with said primer under the same conditions used in step a); and
 - 30 c) amplifying the sampled nucleic acid; and

d)detecting the level of amplified nucleic acid from both patient and control samples; wherein detection of levels of the amplified nucleic acid in the patient sample that differ significantly from levels of the amplified nucleic acid in the control sample is indicative of disease.

5 28. A method according to claim 23 or claim 24 comprising:

a)obtaining a tissue sample from a patient being tested for disease;

b)isolating a nucleic acid molecule according to any one of claims 11 to 14 from said tissue sample; and

c)diagnosing the patient for disease by detecting the presence of a mutation which is 10 associated with disease in the nucleic acid molecule as an indication of the disease.

29. The method of claim 28, further comprising amplifying the nucleic acid molecule to form an amplified product and detecting the presence or absence of a mutation in the amplified product.

30. The method of claim 28 or claim 29, wherein the presence or absence of the mutation 15 in the patient is detected by contacting said nucleic acid molecule with a nucleic acid probe that hybridises to said nucleic acid molecule under stringent conditions to form a hybrid double-stranded molecule, the hybrid double-stranded molecule having an unhybridised portion of the nucleic acid probe strand at any portion corresponding to a mutation associated with disease; and detecting the presence or absence of an 20 unhybridised portion of the probe strand as an indication of the presence or absence of a disease-associated mutation.

31. A method according to any one of claims 23 to 30, wherein said disease includes, but is not limited to, cell proliferative disorders, autoimmune/inflammatory disorders, such as 25 arthritis, cardiovascular disorders, neurological disorders, developmental disorders, metabolic disorders, AIDS, renal disease, infections and other pathological conditions.

32. A method according to any one of claims 23 to 30, wherein said disease is a disease in which members of the leucine rich repeat containing family of proteins are implicated.

33. Use of a polypeptide according to any one of claims 1 to 10 as a member of the leucine rich repeat containing family of proteins.

30 34. A pharmaceutical composition comprising a polypeptide according to any one of

claims 1 to 10, a nucleic acid molecule according to any one of claims 11 to 14, a vector according to claim 15, a host cell according to claim 16, a ligand according to claim 17 or claim 18, or a compound according to any one of claims 19 to 21.

35. A vaccine composition comprising a polypeptide according to any one of claims 1 to 5 10 or a nucleic acid molecule according to any one of claims 11 to 14.

36. A polypeptide according to any one of claims 1 to 10, a nucleic acid molecule according to any one of claims 11 to 14, a vector according to claim 15, a host cell according to claim 16, a ligand according to claim 17 or claim 18, a compound according to any one of claims 19 to 21, or a pharmaceutical composition according to 10 claim 34, for use in the manufacture of a medicament for the treatment of cell proliferative disorders, autoimmune/inflammatory disorders, such as arthritis, cardiovascular disorders, neurological disorders, developmental disorders, metabolic disorders, AIDS, renal disease, infections and other pathological conditions.

37. A polypeptide according to any one of claims 1 to 10, a nucleic acid molecule according to any one of claims 11 to 14, a vector according to claim 15, a host cell according to claim 16, a ligand according to claim 17 or claim 18, a compound according to any one of claims 19 to 21, or a pharmaceutical composition according to claim 34, for use in the manufacture of a medicament for the treatment of a disease in which members of the leucine rich repeat containing family of proteins are implicated.

20 38. A method of treating a disease in a patient, comprising administering to the patient a polypeptide according to any one of claims 1 to 10, a nucleic acid molecule according to any one of claims 11 to 14, a vector according to claim 15, a host cell according to claim 16, a ligand according to claim 17 or claim 18, a compound according to any one of claims 19 to 21, or a pharmaceutical composition according to claim 34.

25 39. A method according to claim 38, wherein, for diseases in which the expression of the natural gene or the activity of the polypeptide is lower in a diseased patient when compared to the level of expression or activity in a healthy patient, the polypeptide, nucleic acid molecule, vector, ligand, compound or composition administered to the patient is an agonist.

30 40. A method according to claim 38, wherein, for diseases in which the expression of the natural gene or activity of the polypeptide is higher in a diseased patient when

compared to the level of expression or activity in a healthy patient, the polypeptide, nucleic acid molecule, vector, ligand, compound or composition administered to the patient is an antagonist.

41. A method of monitoring the therapeutic treatment of disease in a patient, comprising monitoring over a period of time the level of expression or activity of a polypeptide according to any one of claims 1 to 10, or the level of expression of a nucleic acid molecule according to any one of claims 11 to 14 in tissue from said patient, wherein altering said level of expression or activity over the period of time towards a control level is indicative of regression of said disease.
- 10 42. A method for the identification of a compound that is effective in the treatment and/or diagnosis of disease, comprising contacting a polypeptide according to any one of claims 1 to 10, or a nucleic acid molecule according to any one of claims 11 to 14 with one or more compounds suspected of possessing binding affinity for said polypeptide or nucleic acid molecule, and selecting a compound that binds specifically to said 15 nucleic acid molecule or polypeptide.
43. A kit useful for diagnosing disease comprising a first container containing a nucleic acid probe that hybridises under stringent conditions with a nucleic acid molecule according to any one of claims 11 to 14; a second container containing primers useful for amplifying said nucleic acid molecule; and instructions for using the probe and 20 primers for facilitating the diagnosis of disease.
44. The kit of claim 43, further comprising a third container holding an agent for digesting unhybridised RNA.
45. A kit comprising an array of nucleic acid molecules, at least one of which is a nucleic acid molecule according to any one of claims 11 to 14.
- 25 46. A kit comprising one or more antibodies that bind to a polypeptide as recited in any one of claims 1 to 10; and a reagent useful for the detection of a binding reaction between said antibody and said polypeptide.
47. A transgenic or knockout non-human animal that has been transformed to express higher, lower or absent levels of a polypeptide according to any one of claims 1 to 10.
- 30 48. A method for screening for a compound effective to treat disease, by contacting a non-human transgenic animal according to claim 47 with a candidate compound and

determining the effect of the compound on the disease of the animal.

49. A polypeptide according to any one of claims 1 to 10, a nucleic acid molecule according to any one of claims 11 to 14, a vector according to claim 15, a host cell according to claim 16, a ligand according to claim 17 or claim 18, a compound according to any one of claims 19 to 21, or a pharmaceutical composition according to claim 34 for use in IVF, the treatment of fertility related disorders or as a contraceptive.
50. A polypeptide according to any one of claims 1 to 10, a nucleic acid molecule according to any one of claims 11 to 14, a vector according to claim 15, a host cell according to claim 16, a ligand according to claim 17 or claim 18, a compound according to any one of claims 19 to 21, or a pharmaceutical composition according to claim 34 for use in the manufacture of a contraceptive.